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EXAMINER	
KAPUSHOC, STEPHEN THOMAS	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 09/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/086,087	YANG ET AL.	
	Examiner	Art Unit	
	Stephen Kapushoc	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/22/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Please note that the Examiner handling this application has changed and is now Stephen Kapushoc in Art Unit 1634. Please direct any future correspondence regarding this application to the above named Examiner.

Claims 1-8 are pending and examined on the merits.

Applicants amendments of 06/22/2006 have amended claim 1. Claim 9 is cancelled. No claims have been newly added.

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06/22/2006 has been entered.

2. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. The following arguments are either Maintained from the Final rejection of 12/30/2005 or new grounds of rejection presented in this office action, as indicated. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments, remarks, and Declaration follow.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Maintained Rejections

Claim Rejections - 35 USC § 102

3. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Bensimon et al (herein referred to as Bensimon, U.S. Patent 6,054,327, 102(b) date 04/25/2000).

Several aspects of instant claim 1.c have been broadly interpreted by the Examiner. Passing the hybridized DNA complex "from a reservoir in a microfluidic device" is interpreted as moving any portion of the hybridized DNA complex initially in a holding area in a device designed to contain small amounts of liquids. Passing the hybridized DNA complex through a "narrow channel to cause an acceleration of flow through said channel" is interpreted as moving any portion of the hybridized DNA complex through a small passageway, which involves an acceleration of flow through the passageway.

Bensimon teaches a method of analyzing DNA comprising hybridizing the DNA in solution with probes having fluorescent reagents and then detecting the position of the probes after aligning ("causing said hybridized DNA complex to extend into a substantially linear configuration", instant claim 1.c) the DNA (instant claims 1, 5 and 6; see column 16, lines 50-55, and Fig. 6 of Bensimon). Bensimon also teaches that DNA molecules placed in a channel between cover slips can be aligned by the evaporation flow parallel to a moving meniscus in the channel (instant claim 1.c; see column 2, lines 11-12 and column 3, line 22 and Fig. 6 of Bensimon). Regarding this method of aligning DNA described by Bensimon, DNA molecules in a random coil state fixed at a location

in a channel between cover slips is interpreted as the embodiment of the hybridized DNA complex initially being in a "reservoir in a microfluidic device" as recited in instant claim 1.c. In addition, as the meniscus initially moves through the channel between the cover slips, there will be an acceleration of fluid flow in the channel and a portion of the DNA complex will pass through the channel as it extends to a linear configuration (see Fig. 6 of Bensimon). This is interpreted as the embodiment of passing the hybridized DNA complex through a "narrow channel to cause an acceleration of flow through said channel, thereby causing said hybridized DNA complex to extend into a substantially linear configuration;" (recited in instant claim 1.c). Bensimon teaches that the probes used to hybridize to DNA can be oligonucleotides, RNA, DNA, and peptide nucleic acids (instant claims 5 and 6; see column 13, lines 21-23 and 64-65 of Bensimon) which identify a specific sequence of DNA by hybridization. Bensimon also teaches that oligonucleotide probes can be labeled with fluorescent labels and microbeads (instant claims 2-4; see column 11, lines 20-41 and column 14, lines 4-7 of Bensimon). With regard to instant claim 1.d reciting "detecting said optically distinguishable material in a sequential manner along said substantially linear hybridized DNA complex,...", the recitation is interpreted as detecting *one or more* optically distinguishable DNA sequence recognition units in a sequential manner along a substantially linear hybridized DNA complex, which is taught by Bensimon (see column 16, lines 50-55 of Bensimon). Relevant to parts e) and f) of claim 1, Bensimon teaches the analysis of the entire length of a linear labeled nucleic acid molecule (e.g. Fig 8) which allows for determining the sequential order of labels on the target, and specifically teaches the use

of multiple probes to determine the position or size of multiple specific sequences, which is identification of the target DNA molecule.

Response to Remarks

4. The response traverses this rejection.

The Remarks asserts that the plain meaning of the term 'through' requires that the hybridized DNA complex proceeds in one side of the channel and out the other (remarks middle of p.7), and has provided several definitions of the term through. This is not found to be persuasive because while one of the provided definitions (definition 1 from the Compact OED) indicates 'moving in one side and out the other side of (an opening or location)', other provided definitions are less definitive regarding passage of an element out of a defined area. For example the Merriam-Webster definition 3 indicates only 'passage from one end or boundary to another', and the Cambridge on-line definition indicates only 'from one end or side of something to the other'. Thus the plain meaning of the term 'through' does not require passage of the element (i.e. the DNA complex) out of the confines of the required area (i.e. the channel), but only requires some movement within the defined area. For example, the provided definitions and the interpretation of the term 'through' by the examiner would allow for one to describe movement of a ball within a box (without the ball leaving the box) as a 'ball moving through a box', or (as provided in the Remarks) someone walking within the wodds without leaving the woods as 'walking through the woods', or in the case of the Bensimon reference a nucleic acid moving from one side of a channel to the other as

moving 'thtough' the channel. Thus given the lack of any structural requirements in the claim with regard to what is considered a channel, and the broad yet appropriate definition of the term 'through', the Examiner maintains that Bensimon does teach passing a hybridized DNA complex through a channel. And while the Remarks indicate that the specification supports the definition of 'through' as the movement in one side and out the other and points to Fig 1a and 1c, and that the figures indicate that the whole hybridized DNA complex passes in one end of a channel and out the other, while the indicated figures may be considered exemplary they do not assign any definitions to the terms 'through' or 'hybridized DNA complex' that are required for the claims. The Examiner maintains that the claims do not recite any limitations with regard to how much of the DNA complex is passed through the channel and therefore movement of all but the fixed end of the DNA complex through the area between the plates as taught by Bensimon in Fig. 6 can be reasonably interpreted as passing the DNA complex through a narrow channel.

Applicants additionally argue that Figs 1a and 1b support the meanings for the terms 'channel' and 'reservoir' in which these elements are two separate parts of the microfluidic device. As detailed above, the figures do not assign any definitions required by the terms recited in the claims. The Examiner maintains that the claims recite the terms 'reservoir' and 'channel' only as named parts of a microfluidic device with no structural limitations or particular spatial relationship regarding either a 'reservoir' or a 'channel'. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988

F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). However, if the claim recited movement of the DNA complex 'from a reservoir in a microfluidic device *into* a narrow channel', the claim would not specify that the reservoir and narrow channel are necessarily distinct compartments with different structural limitations.

This rejection is maintained.

5. Claims 1-6 are rejected under 35 U.S.C. 102(e) as being anticipated by Chan et al (hereinafter referred to as Chan-1; Pre Grant Publication 2003/0059822, 102(e) date 09/18/2001).

Chan-1 teaches a method of analyzing a polymer comprising labeling the polymer with first and second unit specific makers, the first unit specific marker having a first label and the second unit specific marker including a second label distinct from the first label; exposing the labeled polymer to a detection station to produce distinct detection signals from the first and second labels; and identifying the distinct first and second signals (instant claim 1; see page 1, para 0008 of Chan-1). Chan-1 also teaches that the first unit specific marker can be different than the second unit specific marker, either in its nature or in the polymer unit it recognizes and binds to (instant claim 1; see page 1, para 0009 of Chan-1). Relevant to parts e) and f) of claim 1, Chan-1 teaches determining the sequential order of the labels of the labeled target (e.g. Fig 8) and thus determining the order of the specific sequence of the target to identify the target DNA molecule. Chan-1 also teaches that the first unit specific marker can be identical to the second unit specific marker, yet the first and second unit specific

markers are labeled with distinct labels (instant claim 1; see page 1, para 0009 of Chan-1). Chan-1 also teaches that the polymer is preferably a nucleic acid that is genomic DNA (instant claim 1; see page 2, para 0013 of Chan-1) and that the unit specific marker can be a nucleic acid probe (instant claims 5 and 6; see page 8, para 0076 of Chan-1), or a peptide or polypeptide or peptide-nucleic acids (instant claims 5 and 6; see page 8, para 0077 of Chan-1). Chan-1 teaches that unit specific markers are attached to optically distinguishable labels that include a fluorescent molecule, a radioisotope, an enzyme, a biotin molecule, an avidin molecule, a semiconductor nanocrystal, a semiconductor nanoparticle, a colloid gold nanocrystal, a micro bead, a protein, a peptide, a nucleic acid, a carbohydrate, an antigen, an antibody, etc. (instant claims 2-4; see page 3, para 0015 of Chan-1). Chan-1 teaches that the pattern of binding of the unit specific markers to the polymer may be determined using a variety of systems including a linear polymer analysis system (instant claim 1; see page 3, para 0033 of Chan-1) such as optical mapping or DNA combing. Chan-1 teaches that the unit specific marker (and thus the polymer) can be sequentially exposed to a station, "station" defined as a region where a portion of the polymer is exposed to an energy source in order to produce a signal or polymer dependent impulse, by movement of the marker and the station relative to one another (instant claim 1; see page 12, para 0109 of Chan-1). Chan-1 teaches that the polymer can be aligned and stretched before it reaches the interaction station and that a very effective technique of stretching DNA is to pass the polymer through a tapered microchannel having an obstacle field, followed by a constant-shear section to maintain the stretching obtained and straighten out any

remaining coiling in the polymer (embodiment of "passing said hybridized DNA complex....." in instant claim 1.c; see page 13, para 0125 and page 14, para 0128 of Chan-1). Chan-1 also teaches that pressure flow is the preferred driving force of the DNA through such a microchannel recited above (see page 14, para 0128 of Chan-1). With regard to instant claim 1.d reciting "detecting said optically distinguishable material in a sequential manner along said substantially linear hybridized DNA complex,...", the recitation is interpreted as detecting *one or more* optically distinguishable DNA sequence recognition units in a sequential manner along a substantially linear hybridized DNA complex, which is taught by Chan-1 (see page 1, para 0008 and page 3, para 0033 of Chan-1).

6. Claims 1-8 are rejected under 35 U.S.C. 102(e) as being anticipated by Hannah et al (hereinafter referred to as Hannah; U.S. Patent 6,767,731 B2, 102(e) date 08/27/2001).

Hannah teaches a method of sequencing a target nucleic acid comprising hybridization of the target DNA with probes, which can be oligonucleotides and oligonucleotide analogs that are uniquely and detectably labeled, using a microfluidic device to pass the hybridized nucleic acid through a microchannel to extend it to an approximate linear conformation by hydrodynamic focusing, and detecting the spectral signature of each labeled probe, preferably in sequential order (instant claims 1, 5 and 6; see column 2, lines 38-44 and 51-56, and column 3, lines 3-7 and 9-11 of Hannah). Relevant to parts e) and f) of claim 1, Hannah teaches that the labels of multiple probes

may be detected in a linear fashion (thus sequential detection) to determine the probe order and identify the target DNA molecule (col.17 – Example 3). Hannah also teaches that nucleic acid molecules sequenced by this method can be DNA or RNA (instant claim 1; see column 4, lines 62-65 of Hannah). Hannah also teaches that the probes used for this method can be DNA, RNA, or analog thereof, such as a peptide nucleic acid (instant claims 5 and 6; see column 6, lines 30-34 of Hannah). Hannah also teaches that the probe labels can be fluorescent, luminescent, radioactive, phosphorescent, chemiluminescent, enzymatic, spin, electron dense, mass spectroscopic, semiconductor nanostructures, and quantum dots (instant claims 2-4; see column 8, lines 42-47 and column 10, lines 12-37 of Hannah). Hannah also teaches that photolithography can be used to obtain microchannels for use in linearizing DNA in the range of tens of micrometers wide and deep (instant claims 7-9; see column 12, lines 14-16 of Hannah). With regard to instant claim 1.d reciting "detecting said optically distinguishable material in a sequential manner along said substantially linear hybridized DNA complex,...", the recitation is interpreted as detecting *one or more* optically distinguishable DNA sequence recognition units in a sequential manner along a substantially linear hybridized DNA complex, which is taught by Hannah (see column 2, lines 38-44 and 51-56, and column 3, lines 3-7 and 9-11 of Hannah).

Response to Arguments and 1.131 Declaration regarding the rejection of claims under 25 USC 102(e)

7. The response traverses the rejections of Chan-1 and Hannah via filing of a declaration under 37 C.F.R. §1.131. The declaration asserts that the claimed invention was conceived by Applicants prior to the US filing date of Hannah or Chan-1 as evidenced by the attached notebook page 154 dated 06/05/2001. The declaration further asserts that diligence was exercised in pursuing a patent application from the time of conception to the time of filing. This declaration has been thoroughly reviewed but was not found persuasive to overcome the rejections of Chan-1 and Hannah. The declaration states that 'the claimed invention was conceived in the US before the US filing date of either' of the applied 102(e) references, and provides "notebook page 154" which discloses the steps of: a) attaching different oligonucleotides with different colored beads, b) hybridizing the labeled oligonucleotides with unknown DNA molecule, c) stretching the DNA molecules from random coil to linear confirmation under microscopy by a microfluidic device as shown in Berkeley, d) and recording the order of colored-beads to determine the species of DNA. It is noted that several limitations of the instant claims are not disclosed by "notebook page 154". With regard to claim 1, part c), the "notebook page 154" does not disclose any teachings of a "reservoir" from which the DNA is passed from. In addition claim 1, part c) recites passing the DNA "from a reservoir in a microfluidic device through a narrow channel to cause an acceleration of fluid flow through said channel, thereby causing said hybridized DNA complex to extend into a substantially linear confirmation". The 'notebook page 154' does not teach how the stretching of the DNA relates to the "acceleration of fluid flow through said channel" recited in instant claim 1.

The Declaration (part 8) provides that 'the reference on the notebook page "as shown in Berkeley" refers to a published article "Effect of flow on complex Biological macromolecules in microfluidic devices," by Polly S Shrewsbury, Susan J Muller and Dorian Liepmann published in 2001 in Biomedical Microdevices, 3:3, 225-238 by Kluwer Academic Publishers'. However, the mere reference, on 'notebook page 154', of 'as shown in Berkeley' is not considered specific enough to point to the limitations provided in the Biomedical Microdevices article. There is nothing within the reference to 'as shown in Berkeley' to direct one to the specific provided article. Thus the Examiner maintains that the phrase 'as shown in Berkeley' recited in "notebook page 154", part c) is given no consideration with regard to the applicant's response regarding the Biomedical Microdevices article (provided in the Declaration as Attachment 2) because it remains unclear how such recitation relates to the invention or the provided article. It is noted that while the 'notebook page 154' is provide with a date of Jun 5, 2001, the publication information for the article (vol.3 no.3) appears to indicate a publication date of September 2001. Additionally, even upon review of the provided Biomedical Microdevices article, this article does not address the further limitations of the claims such as microparticles having different shapes (claim 3), nanocrystals (claim 4), peptide nucleic acids (claim 5), or protein scaffolds or synthetic molecular moiety (claim 6); and while the article teaches a channel with the particular dimensions of 300 um wide x 60 um deep, the reference does not teach a range of widths or depths as recited in claims 7 and 8.

The Declaration further provides (as Attachment 3) data from 'Invention Tracker' to indicate that diligence was exercised in pursuing a patent application from the time of conception to the time of filing (parts 9-11 of the Declaration). It is noted that the Attachment 3 provided with the instant Declaration provides no details regarding the recited limitations of the instant claims not provided in the 'notebook page 154'. Additionally, MPEP 715.07(a) states:

> In determining the sufficiency of a 37 CFR 1.131 affidavit or declaration, diligence need not be considered unless conception of the invention prior to the effective date is clearly established, since diligence comes into question only after prior conception is established. Ex parte Kantor, 177 USPQ 455 (Bd. App. 1958).

Thus, because conception of the invention in a scope commensurate with the requirements of the claims has not been established, the point of excercised diligence is moot.

For these reasons and the reasons already made of record, the rejection is maintained.

Newly presented grounds of rejection under 35 USC 102(b)

8. Claims 1, and 5-8 are rejected under 35 U.S.C. 102(e) as being anticipated by Chan et al PCT/US00/22253 (WO 01/13088 publication date 02/22/2001, herein referred to as Chan-2).

Chan-2 provides methods for the sequence analysis of a single nucleic acid molecule by visual examination of a nucleic acid molecule stretched into a linear conformation.

Chan-2 teaches (e.g. page 22) teaches methods comprising extrinsically labeling a target nucleic acid sequence using an oligonucleotide (which is a DNA sequence recognition unit that identifies a specific sequence of DNA in a target, termed in the reference a 'unit specific marker') to which a label such as a fluorescent dye (which is an optically distinguishable material) is attached, relevant to part a) of claim 1. Relevant to part b) of claim 1, Chan-2 teaches that a labeled oligonucleotide can be hybridized to a target DNA to 'mark' a specific target sequence in the target (e.g. page 22), and teaches the target DNA may be 'marked' when it is in a random coil state (e.g. page 45). Relevant to part c) of claim 1, Chan-2 teaches passing the labeled target DNA through a channel in a fluid carrier to cause the target:label complex to extend into a linear conformation (e.g.: p.39 ln.30; p.45 Example 6.2; Figs 9 and 15), and that the effect of accelerated fluid flow causes the target DNA to extend (e.g.: p.29 - Branched Channels; p.27 – Funnel Structures). Relevant to part d) of claim 1, Chan-2 teaches the detection of the labels on the target DNA along the length of the target (e.g. Figs 26-28; p.45 lns.1-11) thus allowing for the sequential detection of the label. Relevant to parts e) and f) of claim 1, Chan-2 teaches that the method can be used to analyze polymers to determine polymer sequence (e.g. p.22 lns.28-33), which is a determination of the sequential order of the labels of the DNA sequence recognition unit thereby identifying the target DNA molecule.

Regarding claims 5 and 6, Chan-3 teaches that the specific sequence recognition elements may be PNAs (p.22 lns.18-20, relevant to claim 5), or sequence specific major or minor groove binders or DNA binding proteins (p.22 lns.17-19, relevant to claim 6).

Regarding claims 7 and 8, Chan-3 teaches that a channel may have a width from 2 um to 1 mm and depths from 0.1 um to 10 um (e.g. p.27 lns.14-15) which satisfies the size limitations of claim 7 (about 0.1 um to about 500 um) and claim 8 (about 1 um to about 300 um).

Response to Remarks

9. Though the rejection of claims under 35 USC 102(b) as anticipated by Chan-2 is a new grounds of rejection, it is relevant to respond to the Remarks of 06/22/2006 regarding the teachings of this reference. Applicants have argued (p.19 of Remarks) that Chan-2 does not disclose or suggest passing a hybridized DNA complex as presently claimed from a reservoir n a microfluidic device through a channel to sequence the target DNA molecule thereby allowing identification of the target molecule. The Examiner asserts that Chan-2 does teach a hybridized DNA complex (e.g. the reference teaches hybridization of a labeled oligonucleotide to a target nucleic acid to label the target in a sequence specific manner (p.22)), and teaches passing labeled target DNA through a channel (e.g. Fig 9) and includes structural elements that are reservoirs (e.g. p.44 lns.22-23, Figs 15 and 25), and specifically teaches determining the sequence of a labeled target nucleic acid and determination of the patterns of unit-specific markers on a labeled polymer (e.g. page 22) which is the identification of the target.

Maintained Rejections

Claim Rejections - 35 USC § 103

10. Claims 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan-1, in view of Chan-2 et al (hereinafter referred to as Chan-2; PCT/US00/22253, International Publication Number WO 01/13088 A1, International Publication Date 02/22/2001).

Chan-1 teaches a method of analyzing a polymer comprising labeling the polymer with first and second unit specific makers, the first unit specific marker having a first label and the second unit specific marker including a second label distinct from the first label; exposing the labeled polymer to a detection station to produce distinct detection signals from the first and second labels; and identifying the distinct first and second signals (instant claim 1; see page 1, para 0008 of Chan-1). Chan-1 also teaches that the first unit specific marker can be different than the second unit specific marker, either in its nature or in the polymer unit it recognizes and binds to (instant claim 1; see page 1, para 0009 of Chan-1). Chan-1 also teaches that the first unit specific marker can be identical to the second unit specific marker, yet the first and second unit specific markers are labeled with distinct labels (instant claim 1; see page 1, para 0009 of Chan-1). Chan-1 also teaches that the polymer is preferably a nucleic acid that is genomic DNA (instant claim 1; see page 2, para 0013 of Chan-1) and that the unit specific marker can be a nucleic acid probe (instant claims 5 and 6; see page 8, para 0076 of Chan-1), or a peptide or polypeptide or peptide-nucleic acids (instant claims 5 and 6; see page 8, para 0077 of Chan-1). Chan-1 teaches that unit specific markers are attached to optically distinguishable labels that include a fluorescent molecule, a radioisotope, an enzyme, a biotin molecule, an avidin molecule, a

semiconductor nanocrystal, a semiconductor nanoparticle, a colloid gold nanocrystal, a micro bead, a protein, a peptide, a nucleic acid, a carbohydrate, an antigen, an antibody, etc. (instant claims 2-4; see page 3, para 0015 of Chan-1). Chan-1 teaches that the pattern of binding of the unit specific markers to the polymer may be determined using a variety of systems including a linear polymer analysis system (instant claim 1; see page 3, para 0033 of Chan-1) such as optical mapping or DNA combing. Chan-1 teaches that the unit specific marker (and thus the polymer) can be sequentially exposed to a station, "station" defined as a region where a portion of the polymer is exposed to an energy source in order to produce a signal or polymer dependent impulse, by movement of the marker and the station relative to one another (instant claim 1; see page 12, para 0109 of Chan-1). Chan-1 teaches that the polymer can be aligned and stretched before it reaches the interaction station and that a very effective technique of stretching DNA is to pass the polymer through a tapered microchannel having an obstacle field, followed by a constant-shear section to maintain the stretching obtained and straighten out any remaining coiling in the polymer (embodiment of "passing said hybridized DNA complex....." in instant claim 1.c); see page 13, para 0125 and page 14, para 0128 of Chan-1). Chan-1 teaches that pressure flow is the preferred driving force of the DNA through such a microchannel recited above (see page 14, para 0128 of Chan-1). With regard to instant claim 1.d) reciting "detecting said optically distinguishable material in a sequential manner along said substantially linear hybridized DNA complex,...", the recitation is interpreted as detecting *one or more* optically distinguishable DNA sequence recognition units in a sequential manner along

a substantially linear hybridized DNA complex, which is taught by Chan-1 (see page 1, para 0008 and page 3, para 0033 of Chan-1).

Chan-1 teaches stretching DNA by passing the DNA through a microchannel, but is silent with respect to the width or depth of the channel (see page 13, para 0125 and page 14, para 0128 of Chan-1). However, Chan-2 teaches that a channel with 1 μm depth, 1 mm length, and a shear rate of 0.25/s gives a force of approximately 0.25 pN, which the inventors have verified experimentally is adequate to stretch DNA (instant claims 7 and 8; see page 25, line 16 of Chan-2). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to perform the method of Chan-1 with the device of Chan-2 because Chan-2 specifically teaches a device for performing the method of Chan-1. The ordinary artisan would have been motivated to use the device of Chan-2 because Chan-1, while generally teaching a method of stretching DNA with a microfluidic device, is silent with regard to the specific structure and dimensions of the device. The device, with its specific dimensions, taught by Chan-2 functions to stretch DNA as taught by Chan-1. The ordinary artisan would be motivated to use the device of Chan-2 in the method of Chan-1 because Chan-1 teaches to stretch DNA by passing the DNA through a microchannel, but no specific structure or dimensions of the microchannel are recited.

Response to Arguments

11. The response traverses this rejection via filing of a declaration under 37 C.F.R. §1.131. For the reasons discussed in the Section numbered 7 above, this declaration

does not over come the rejection by Chan-1 with regard to claims 1-6. With regard to the further limitations of claims 7 and 8, it is noted that the Declaration does not provide teachings encompassing the range of dimensions of the channel of the microfluidic device. For these reasons and the reasons already made of record, the rejection is maintained.

Newly presented grounds of rejection under 35 USC § 103

12. Claims 2-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al PCT/US00/22253 (WO 01/13088 publication date 02/22/2001, herein referred to as Chan-2) in view of Bensimon et al (U.S. Patent 6,054,327).

As discussed in the section numbered 8 of this office action, Chan-2 teaches a method for single molecule identification of a target DNA comprising all of the limitations of claim 1, from which rejected claims 2-4 depend.

Chan-2 does not specifically teach the labeling of oligonucleotide probes with microparticles.

Bensimon teaches methods for the analysis of linearized target nucleic acid molecules using oligonucleotide probes, and teaches that oligonucleotide probes can be labeled with fluorescent labels and microbeads (instant claims 2-4; see column 11, lines 20-41 and column 14, lines 4-7 of Bensimon).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the oligonucleotide labeling techniques taught by Bensimon et al to analyze oligonucleotide probes hybridized to target DNA

molecules in the methods of Chan-2. One would have been motivated to use the techniques of Bensimon et al based on the assertion of Bensimon that such methods are suitable for the detection of probes hybridized to a single target DNA molecule stretched into a linearized conformation.

Conclusion

13. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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